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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	**PAPER NUMBER**
1616	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/657,550	CHAUDRY, IMTIAZ	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-70* is/are pending in the application.

4a) Of the above claim(s) *2, 7-9, 16-21, 31-34, and 36-70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,10-15,22-30 and 35* is/are rejected.

7)☒ Claim(s) *3 and 30* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/7/06; 9/8/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-70 are pending. Claims 2, 7-9, 16-21, 31-34, and 36-44 are withdrawn as being drawn to a non-elected species. Claims 45-70 are withdrawn as being drawn to a non-elected invention. **Claims 1, 3-6, 10-15, 22-30, and 35 are under consideration in the instant office action.** Receipt and consideration of Applicant's response to the restriction/species requirement submitted on February 16, 2007 is acknowledged.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-44) in the reply filed on February 16, 2007 is acknowledged. The traversal is on the ground(s) that the burden placed on the Applicant in having to file and prosecute separate applications for the inventions of Group I and II outweighs the burden placed on the Examiner in searching the groups together. This is not found persuasive because this Examiner has limited time allowed to search a given application and communicate the findings of his searches to Applicant regarding the merits of the instant Application. Thus, a search of both Groups I and II would represent a serious burden to the Examiner, because the searches are not expected to be coextensive as set forth in the restriction requirement mailed on October 16, 2006.

The requirement is still deemed proper and is therefore made FINAL.

Specification

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claims 3 and 30 are objected to because of the following informalities: (1) claim 3 ends in two periods, which is grammatically incorrect; and (2) the names of drugs are incorrectly capitalized in claim 30, because the name of a chemical compound is not a proper noun. According to proper English grammar, only proper nouns or words at the beginning of a sentence are capitalized. Appropriate correction is required.

The use of the trademark THE PHYSICIAN'S DESK REFERENCE® ([0041]) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1, 3-6, 10-15, 26-28, and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because it refers to a pharmaceutically acceptable derivative of fluticasone; however, the specification does not define what Applicant considers a pharmaceutically acceptable fluticasone derivative. The 10th edition of the Merriam-Webster's Collegiate Dictionary (Merriam-Webster Incorporated: Springfield, Massachusetts, 1993, pp 311) defines "derivative" as, "a chemical substance related structurally to another substance and theoretically derivable from it." For example, carbon dioxide could theoretically be derived from the combustion of fluticasone. Therefore, the definition of derivative in the Merriam-Webster Collegiate Dictionary does not shed light on what Applicants' intended for the meaning of a fluticasone derivative. Thus, an ordinary skilled artisan would not be apprised of the metes and bounds of the term "derivative."

Claim 26 is confusing and as a result indefinite, because it is impossible for particulate fluticasone that is dissolved (i.e. in an aqueous solution) to have the particle size distribution described in parent claim 1. It is also noted that it is physically impossible for dissolved fluticasone propionate to exist as particles having the claimed sizes of (a) less than 0.9 microns, (b) less than 1.6 microns, (c) less than 3.2 microns, (d) less than 6.2 microns, and (e) less than 10.0 microns, because, although one could consider an individual molecule of fluticasone to be a particle, its size is inherently several orders of magnitude smaller than the ranges claimed by Applicants.

The remaining claims are rejected for depending upon a rejected claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3-6, 10-15, 22-26, and 28-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Osbakken et al. (US 2002/0061281) in view of Waldrep et al. (U.S. Patent No. 5,958,378), Lancaster et al. (WO 02/00199; IDS), and Ferrie et al. (WO 01/32125; IDS).

It is noted that several composition claims recite intended uses of the given composition, however, the intended use of composition claims is given little weight in examination of compositions. Osbakken does not anticipate the cited claims because this reference does not expressly teach the claimed particle size distribution.

Applicant Claims

Applicant claims a formulation comprising (a) 1-700 micrograms of a steroidal anti-inflammatory that is fluticasone or an acceptable derivative thereof characterized by the particle size distribution described in claim 1, further comprising (b) an antifungal (e.g. claims 3-6), or (c) a preservative, such as benzalkonium chloride (e.g. claims 23-24 and 28), or (d) an antibiotic (e.g. doxycycline) (e.g. claims 29-30).

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Osbakken teaches **pharmaceutical compositions** are described that comprise one or more active ingredients including an **anti-infective agent, anti-inflammatory agent, and antibiotic combinations** or combinations of others of these classes of ingredients, especially compositions **formulated as a solution or suspension** in a unit dose for aerosol administration to treat chronic sinusitis (abstract).

Osbakken teaches that sinusitis is an inflammation of the membrane lining one or more **paranasal sinuses (i.e. paranasal mucosa)**, and there are three principle kinds of sinusitis: acute, recurrent acute, and chronic [0004]. Therefore, it is obvious that the term rhinosinusitis encompasses sinusitis as in a genus-species relationship, wherein sinusitis is a species of the genus rhinosinusitis. Species are obvious over the genius.

Osbakken teaches that bacteria commonly associated with acute sinusitis, and that, although less common fungal sinusitis does occur and is often associated with infections caused *by Aspergillus, Vurvularia, Bipolaris, Exserohilum, Metarrhizium anisopliae,* and *Mucormycosis*

fungi [0007]-[0008]. The primary objectives for the treatment of sinusitis are reduction of swelling, eradication of infection, draining of the sinuses, and ensuring that the sinuses remain open [0015]. Nebulization therapy is a conventional treatment for pulmonary infections and is also known to have been **used for sinus infections**, with few systemic side effects [0026].

Osbakken teaches that it had been suggested previously in the prior art to use small **aerosol particles of about 2-4 microns** in the treatment of sinusitis. See [0027]-[0029], especially [0029].

Osbakken teaches that the use of synergistic antibiotic combination is desirable; because it allows for the treatment of more difficult infections (e.g. infections due to multiple-antibiotic-resistant organisms) and lower dosages, thereby reducing the probability of toxicity complications, treatment time, and therapy cost. For example, **cefuroxime and gentamicin**, either individually or in combination with other agents, have been used to treat patients with sinusitis [0066]-[0068].

Osbakken teaches that his invention involves the **topical delivery of medications to the nasal cavity and sinuses** by aerosolizing **aqueous solutions or suspensions** of the medications taught. The aerosolized anti-infective particles are surprisingly effective when they have a mass median aerodynamic diameter (MMAD) of about 1.0 to 5.0 microns [0081]. Aerosolization/atomization of the formulations for nasal inhalation by a patient will result in liquid aerosol cloud particles having a MMAD of preferably between **about 0.5 microns and 10 microns**. Examples of suitable medicaments include **amphotericin beta (anti-fungal), cefuroxime (antibiotic), ciprofloxacin (antibiotic), tobramycin (antibiotic), cefoperazone (antibiotic), erythromycin (antibiotic), gentamycin (antibiotic)** [0085], **fluticasone (anti-**

inflammatory), and beclomethasone (anti-inflammatory) [0139]. An exemplary formulation is described in [0178] and comprises **amphotericin beta (10 mg unit dose)**, hydrocortisone sodium succinate (50 mg dose in 3 ml sterile water) together with an anti-inflammatory agent. **Preferable dosage ranges** of various active agents including **amphotericin beta, beclomethasone, fluticasone, fluconazole, itraconazole, aztreonam, cefepime, doxycycline, tobramycin, vancomycin**, etc. are taught in Table-1.

Osbakken teaches that if necessary, osmotic pressure may then be raised to fall within a preferred range **by adding NaCl, dextrose, or other salts** to the liquid [0096]. Surfactants can be used as dispersing agents, solubilizing agents, and spreading agents. Some examples of surfactants are: PEG 400, sodium lauryl sulfate, spans (20-40-60 etc), tweens (**polysorbates, 20-40-60 etc**), tyloxapol, propylene glycol, and **benzalkonium chloride**. Benzalkonium chloride is also a preservative.

Osbakken teaches in [0104] a general preparation of his invented formulations, wherein after determining the medications to be used in the formulation, each ingredient is weighed/measured individually, added together, mixed with diluent (e.g. **sterile water**), filtered with a coarse filter, and then a fine filter (5 micron, 2 micron, 1 micron, 0.45 micron, or 0.22 micron). The preparation is tested to ensure it is within the established parameters for surface tension, osmolarity, pH, and sodium chloride equivalency. To prepare a unit dose, the ingredients of such formulations generally will be dissolved in a solvent such as water or saline solution, in a volume between about 0.5 and 6.0 ml.

Osbakken teaches a **method of treating a mammal suspected or diagnosed as having chronic sinusitis** comprising the step of **administering** to the patient the pharmaceutical

composition of any one of claims 1 or 2, by aerosolization using a nebulizer, which delivers aerosol particles of between about 1 to 5 microns in average diameter in claim 16 of US-2002. Osbakken also teaches in [0235] that **the medication is nebulized three times daily** and that the therapeutic treatment was continued for a total of seven days.

Waldrep's figures 1 and 3 depict the particle size distribution of liposomal aerosol compositions of cyclosporin A (an antifungal agent) and budesonide (an anti-inflammatory steroid), respectively, that are characterized by MMAD values of 1.6 and 2.0 for two different cyclosporin A compositions and MMAD values for two different budesonide compositions of 1.2 and 2.0. Waldrep's figures clearly teach that MMAD is art recognized as representing the central point in a distribution of particle sizes.

Lancaster clearly demonstrates that art recognized methods of preparing pharmaceutical particulate particles yields a composition comprising a distribution of particle sizes, which Lancaster describes using a median particle size (D50), particle size at 90% undersize (D90), and particle size at 10% undersize (D10) (see table on pg. 13). Likewise, Ferrie's figure 2, clearly demonstrates that particulate medicament compositions made by methods known in the art obviously are comprised of distributions of particle sizes.

Ascertainment of the Difference Between Scope the Prior Art and the Claims

(MPEP §2141.012)

Osbakken lacks the express teaching of specific particle size distributions. This deficiency is obviated by Osbakken's teaching of MMAD ranges overlapping the particle sizes

claimed by Applicant and the general knowledge in the art, as demonstrated by the teachings of Waldrep, Lancaster, and Ferrie.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention that the cited claims of the instant application are obvious over the teachings of Osbakken et al. It would have been apparent to a skilled artisan that the method of Osbakken involves the application of his invented formulations to the paranasal mucosa, because sinusitis is a condition characterized by the inflammation of the membrane lining one or more paranasal sinuses (i.e. paranasal mucosa). Furthermore, Osbakken teaches topical delivery of medications to the nasal cavity and sinuses by aerosolizing aqueous solutions or suspensions of the medications. It would have been apparent to a skilled artisan at the time of the instant invention to optimize the particle size distribution of anti-inflammatory particles, because the physical characteristics (e.g. size and shape) of particulate compositions are clearly result specific parameters that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal physical particle characteristics (e.g. particle size and particle size distribution.) of a particulate composition needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention. It is noted that Applicant's specification does not contain any data regarding the properties of the claimed compositions, but merely

tabulated exemplified compositions. Applicant's specification is devoid of allegations of surprising or unexpected results. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Claims 27 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Osbakken et al. (US 2002/0061281; IDS) in view of Waldrep et al. (U.S. Patent No. 5,958,378), Lancaster et al. (WO 02/00199; IDS), and Ferrie et al. (WO 01/32125; IDS) as applied to claims 1, 3-6, 10-15, 22-26, and 28-30 above, and further in view of Bernini et al. (U.S. Patent No. 6,464,958; IDS).

Applicant Claims

Applicant claims a formulation as described above in the instant application wherein said formulation is in a metered-dose spray pump bottle and/or wherein the anti-inflammatory steroid is fluticasone propionate.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Osbakken, Waldrep, Lancaster, and Ferrie have been set forth above in the instant office action. Bernini teaches a process for the preparation of suspensions of drug particles for **inhalation delivery**, providing **optimized particle size and distribution**. A further aspect of the invention is directed to a process for preparing micronized **sterile steroidal formulations** by gamma-irradiation (abstract; col. 1, lines 17-27; col. 4, lines 14-25).

Bernini teaches that a number of **inhalation formulations** have been marketed for some years for the administration of **steroidal anti-inflammatory agents** for the topical **treatment of rhinitis and/or sinusitis**. An example of these steroidal anti-inflammatory drugs includes **beclomethasone dipropionate** (BDP). These formulations can be administered in the form of a finely divided (i.e. micronized powder) **suspension in an aqueous phase** containing necessary surfactants (i.e. emulsifiers) and/or cosolvents. When intended for administration in the form of **metered dose aerosol sprays**, these sprays should also contain **a low-boiling propellant** (col. 1, lines 8-12, 17-20, 22-26).

Bernini teaches that in the process of preparing her formulations an **aqueous solution**, which constituted the carrier optionally, contains **wetting agents, surfactants** (i.e. emulsifiers), **preservatives, stabilizing agents, buffers**, and can optionally be **sterilized**.

Bernini teaches that the degree of solid particle size reduction and the resulting particle size distribution of the formulations produced by her process can be optimized by controlling several variables: (i) the type and size of the interaction chamber; (ii) the operating pressure; and (iii) the processing time and the number of cycles the material passed through. The process effects are also dependent on the physicochemical properties of the ingredients subjected to treatment, however pressure and process times can be modified to achieved the desired results (col. 2, lines 33-43).

Bernini teaches that it would be highly advantageous to provide aqueous suspensions of steroids to be delivered in single unit-dose preparations, because **sterility** is a requirement in greater demand for pharmaceutical formulations intended for **nebulization** (col. 4, lines 31-36).

Bernini teaches that BDP micronized formulations when subjected to gamma radiation at 2 to 9 KGy remain chemically stable (col. 5, lines 53-55). Bernini states that the invented method allows for the preparation of sterile micronized BDP suspensions (col. 6, lines 19-21). Other drugs, which can be used in Bernini's formulations and methods, include corticoid steroids, such as **fluticasone propionate**, and other inhalable anti-inflammatory steroids (col. 1, lines 17-27; col. 4, lines 14-25; claims 1, 2, and 5-6).

Bernini teaches that the BDP starting material used in her process has a particle size of less than 10 microns, **preferably less than 5 microns**. The formulations for inhalation resulting from her invented process can be used to treat any **allergic** and/or inflammatory **condition of the nose** or the lungs (col. 6, lines 33-43).

Ascertainment of the Difference Between Scope the Prior Art and the Claims

(MPEP §2141.012)

Osbakken, Waldrep, Lancaster, and Ferrie lack the teaching of compositions in a metered-dose pump spray this deficiency is cured by the teachings of Bernini.

Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to combine the teachings of Osbakken and Bernini, because both inventors teach compositions comprising anti-inflammatory compounds (e.g. fluticasone) for nasal administration to treat sinusitis. A skilled artisan would have been motivated to combine the teachings of Osbakken with Bernini, because Bernini also teaches methods of making sterile

formulations and it is highly desirable in pharmaceutical formulations intended for nebulization and both sinusitis and rhinitis may be caused by microbial (bacterial or fungal) infections. The use of fluticasone propionate would have been obvious to a person of ordinary skill in the art at the time of the instant invention, because it is a well-known ester derivative of fluticasone (See, for example, Lacy, C.; Armstrong, L. L.; Lipsy, R. J.; Lance, L. L. *Drug Information Handbook*, Lexi-Comp, Inc.: Cleveland, 1993, pp 397) and Bernini teaches fluticasone propionate as a suitable drug for use in the invented suspensions/solutions. The use of a metered-dose pump spray to administer therapeutically effective compositions to treat rhinosinusitis would have been apparent to a skilled artisan cognizant of the teachings of Osbakken and Bernini, because Bernini teaches that compositions in the form of metered-dose aerosol sprays should also contain low boiling propellant. It would have been apparent to a person of ordinary skill to modify the particle size distribution of a composition comprising beclomethasone to obtain an optimized particle size distribution profile, because it is well known in the art that the particle size distribution of an aerosolized drug composition is very important to the therapeutic efficacy of the drug when delivered by inhalation. The physical characteristics (e.g. size and shape) of particulate compositions are clearly result specific parameters that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal physical particle characteristics (e.g. particle size and particle size distribution.) of a particulate composition needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention.

It would also have been apparent to a skilled artisan that one would modify the dosage frequency according to the needs of the subject suffering from rhinosinusitis, the severity of rhinosinusitis in said subject, and the observed effectiveness of a given regimen for the treatment of rhinosinusitis. It is noted that Applicant's specification does not contain any data regarding the properties of the claimed compositions, but merely tabulated exemplified compositions. Applicant's specification is devoid of allegations of surprising or unexpected results. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 10-15, and 22-28 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-6, 9-20, and 23 of copending Application No. 11/078,263 (copending '263). Although the conflicting claims are not identical, they are not patentably distinct from each other because they are overlapping in scope, and/or obvious over one another, and the dependent claims recite similar formulation properties and excipients. The claims of the instant application have been described above. Independent claim 1 of copending '263 claims a formulation comprising an anti-inflammatory. Fluticasone propionate is a known anti-inflammatory drug, as evidenced by dependent claim 6 of copending '263. The cited dependent claims of the instant application and copending '263 have the same, substantially overlapping, and/or obvious limitations.

This is a provisional obviousness-type double patenting rejection.

Claims 1, 10-13, and 22-28 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4, 6-10, 11-14, and 19 of copending Application No. 11/250,256 (copending '256) in view of Bernini et al. (U.S. Patent No. 6,464,958). Although the conflicting claims are not identical, they are not patentably distinct from each other because they are overlapping in scope, and/or obvious over one another, and the dependent claims recite similar formulation properties and excipients. The cited claims of the instant application are drawn to formulations comprising a "steroidal anti-inflammatory (e.g. fluticasone)" having specific particle size distribution profiles that are the same, or overlap with, and/or are obvious over the particle size distribution profiles (PSDP) recited in claims 1, 4, 6-10, 11-14, and 19 of copending 256. Beclomethasone, recited in the cited claims of copending

'256, is a steroidal anti-inflammatory. Although the cited claims of the instant application recite a different anti-inflammatory steroid (i.e. fluticasone), it is the Examiner's position that (1) the anti-inflammatory drug of copending '256 (i.e. beclomethasone) reads on "a pharmaceutically acceptable [fluticasone] derivative" and (2) obviates fluticasone propionate, because (1) both fluticasone propionate and beclomethasone share the same active steroidal core structure and (2) Bernini teaches that beclomethasone and fluticasone are known anti-inflammatory steroids. Regarding the amounts of drug substance and the differences in PSDP, the physical characteristics (e.g. size and shape) of particulate compositions and the amounts of individual components are clearly result specific parameters that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal physical particle characteristics (e.g. particle size distribution) of a particulate composition and the optimal amount of the different compositions ingredients needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts and PSDP would have been obvious at the time of applicant's invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 3-6, 10-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 7-8, 10, and 14-19 and 17-30 of copending Application No. 11/250,925 (copending '925) in view of Bernini et

al. (U.S. Patent No. 6,464,958). Although the conflicting claims are not identical, they are not patentably distinct from each other because they are overlapping in scope and/or are contain substantially similar limitations. Both applications are drawn to formulations and methods intended for the treatment of rhinosinusitis, wherein said formulations comprise a steroidal anti-inflammatory agent and an anti-fungal compound. Both applications also recite substantially similar particle size distribution profiles for the anti-inflammatory drug. The dependent claims of both applications also identify amphotericin beta as the anti-fungal agent and further limit the amount of the different actives. One difference between applications is that copending '925 recites claims drawn to a nasal spray formulation and the instant application does not. This deficiency is cured by the teachings of Bernini set forth above, regarding pharmaceutical formulations comprising an anti-inflammatory steroid in the form of a spray for nasal administration, in one embodiment through the use of a metered-dose aerosol spray formulation. Regarding the amounts of actives recited in both applications, the amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Terminal Disclaimers

It is noted for the record that a terminal disclaimer over the instant application was filed (6/28/2006) and approved (9/29/2006) during the prosecution of copending application 11/250,220.

Conclusion

Claims 1, 3-6, 10-15, 22-30, and 35 are rejected. Claims 3 and 30 and the specification are objected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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